Gp 1642 #12 DMT 2-8-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit	: 1643
Examiner	: B. Tedeschi
Serial No.	: 09/481,990
Filed	: January 11, 2000
Inventor	: Florian Lesage
	: Eric Guillemare
	: Michael Fink
	: Fabrice Duprat
	: Michel Lazdunski
	: Georges Romey
	: Jacques Barhanin
Title	: FAMILY OF MAMMALIAN POTASSIUM CHANNELS, THEIR CLONING AND THEIR USE, ESPECIALLY FOR THE SCREENING OF DRUGS

Docket: 1201-DIV-00
(Formerly 989.6351DIV)

Dated: December 14, 2001

Commissioner for Patents
Washington, DC 20231

Sir:

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Response

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By: _____

Date: 14 DEC 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

22469

PATENT TRADEMARK OFFICE

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RESPONSE

Commissioner for Patents
Washington, D.C. 20231

Sir:

We note with appreciation the withdrawal of the objection to the Specification and the rejection under 35 U.S.C. §112, second paragraph.

Claims 9, 11, 12 and 15-19 are solicited.

Turning to the merits of the application, we respectfully submit that utility of the invention has been established on the record.

The statutory basis for the utility requirement resides in 35 U.S.C. §101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor....

Thus, §101 serves two purposes: it defines which categories of inventions are eligible for patent protection and ensures that patents are granted on only those inventions that are "useful." Deficiencies of the utility requirement arise in two forms: failure to identify any specific and substantial utility for the invention or to disclose sufficient information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention; *see* Brenner v. Manson, 383 U.S.P.Q.519 (1966); and an incredible assertion of specific and substantial utility of the invention by an applicant. Therefore, where the claimed invention has a well-established utility such that a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention, and the utility is specific, substantial and credible, a rejection based on lack of utility is improper. *See* MPEP §2107.

A statement of specific and substantial utility will usually explain "the purpose of or how the invention may be used (e.g., a compound is believed to be useful in the treatment of a particular disorder)." MPEP §2107.02. "Specific utility" is utility that is specific to the subject matter claimed. For example, while a general statement of diagnostic utility such as diagnosing an unspecified disease is insufficient, disclosure of a specific biological activity that reasonably correlates to a disease condition is sufficient to identify a specific utility for the invention. A "substantial utility" defines a "real world" use. For example, a therapeutic method of treating a known disease has "substantial utility". MPEP §2107.01.

Moreover, if the asserted utility is "credible (i.e., believable based on the record or the nature of the invention), a rejection based on 'lack of utility' is not appropriate. Clearly, Office personnel should not begin an evaluation of utility by assuming that an asserted utility

is likely to be false, based on the technical field of the invention or for other general reasons.... Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (i.e. 'question') the truth of the statement of utility." MPEP §2107.02.

In the instant case, a specific, substantial, and credible utility has been asserted. The instant claims are not "drawn to a protein which has a yet undetermined function or biological significance." Rather, the Specification provides substantial evidence as to the biological significance of the TWIK-1 protein encompassed by Claims 11 and 12. As shown in Fig. 2a, the TWIK-1 protein shares the signature P domain of other known potassium (K+) channels. Moreover, sequence alignment data and hydrophobicity studies revealed that the TWIK-1 protein has 2 P domains and 4 transmembrane domains. Contrary to the conclusion that sequence similarity is insufficient to establish the biological activity of the TWIK-1 proteins, evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility is sufficient to support an assertion of therapeutic utility for a new compound. *See In re* Jolles, 206 U.S.P.Q. 885 (CCPA 1980) (finding utility on the basis of a close structural relationship and shared pharmacological activity between a claimed compound and known compounds); MPEP §2107.03.

Moreover, *in vitro* data is sufficient to establish therapeutic utility for a compound, composition, or process. *See* MPEP §2107.03. In the present case, *in vitro* studies revealed the biological role of TWIK-1. Specifically, TWIK-1 is K+ selective and exhibits weak inward rectification. Additionally, TWIK-1 activity was shown to be sensitive to intracellular acidification and phosphorylation by protein kinase C. Thus, even assuming

arguendo that sequence similarity to proteins of known activity is insufficient to establish biological significance, more than enough experimental evidence supports the role of the TWIK-1 proteins as potassium channels.

While inventions asserted to have utility in a treatment of human or animal disorders are subject to the same legal requirements for utility as any other field, pharmacological or therapeutic inventions that provide any "immediate benefit to the public" satisfy 35 U.S.C. §101. Nelson v. Bowler, 206 U.S.P.Q. 881, 883 (CCPA 1980). One having ordinary skill in the art can readily appreciate the therapeutic value of the claimed invention. As stated on pages 14-15 of the Specification, cells expressing a member of the TWIK-1 family of proteins are useful for screening for substances capable of regulating activity of the TWIK-1 potassium channels, thus making possible the identification of drugs for the treatment of diseases of the heart or nervous system, specifically diseases "involving potassium channels, such as epilepsy, heart (arrhythmias) and vascular diseases, neurodegenerative diseases, especially those associated with ischemia or anoxia, the endocrine diseases associated with anomalies of hormone secretion, and muscle diseases." Discovery of the TWIK-1 protein and its gene further allow development of transgenic models for studying diseases associated with the TWIK-1 potassium channels and genetic therapy strategies aimed at correcting deficiencies of the potassium channels. Elucidation of the chromosomal location of the TWIK-1 gene allows prenatal diagnosis of TWIK-1 associated diseases. Pharmaceutical compositions comprising a TWIK-1-type protein, or an antibody directed against it, are useful for the diagnosis, treatment, or prevention of diseases involving dysfunction of potassium channels. In light of the structural similarity and the substantial data provided in

the Specification, it has not been established on this record that it is more likely than not that one having ordinary skill in the art would doubt or question the truth of the asserted utility. In short, a credible therapeutic utility is well-established on the record.

This is not a case in which the biological significance of the invention is not known. In sharp contrast, the specific biological activity of the TWIK-1 family of proteins as potassium channels has been well-established on the record. Moreover, in contrast to a general statement of diagnostic utility, the specific biological activity of the TWIK-1 protein is reasonably correlated to specific disease conditions associated with potassium channels. Additionally, many "real world" uses have been provided. Furthermore, one of ordinary skill in the art would immediately appreciate the usefulness of the claimed invention based on the protein characteristics set forth in the Specification.

In short, we respectfully submit that the utility of the invention is well-established on the record. As such, we respectfully submit that the invention as defined by Claims 11 and 12 is enabled.

In light of the foregoing, we submit that Claims 11 and 12 are in proper form for allowance, and we accordingly urge rejoinder of the solicited method Claims 9 and 15-19, which actions are hereby respectfully requested.

Respectfully submitted,

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